

# Psychiatric manifestations of neurocysticercosis: a study of 38 patients from a neurology clinic in Brazil

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## Abstract

**Objective**—To determine the frequency and features of psychiatric morbidity in a cross section of 38 outpatients with neurocysticercosis.

**Methods**—Diagnosis of neurocysticercosis was established by CT, MRI, and CSF analysis. Psychiatric diagnoses were made by using the present state examination and the schedule for affective disorders and schizophrenia—lifetime version; cognitive state was assessed by mini mental state examination and Strub and Black's mental status examination.

**Results**—Signs of psychiatric disease and cognitive decline were found in 65.8 and 87.5% of the cases respectively. Depression was the most frequent psychiatric diagnosis (52.6%) and 14.2% of the patients were psychotic. Active disease and intracranial hypertension were associated with higher psychiatric morbidity, and previous history of mood disorders was strongly related to current depression. Other variables, such as number and type of brain lesions, severity of neuropsychological deficits, epilepsy, and use of steroids did not correlate with mental disturbances in this sample.

**Conclusions**—Psychiatric abnormalities, particularly depression syndromes, are frequent in patients with neurocysticercosis. Although regarded as a rare cause of dementia, mild cognitive impairment may be a much more prevalent neuropsychological feature of patients with neurocysticercosis. The extent to which organic mechanisms related to brain lesions may underlie the mental changes is yet unclear, although the similar sex distribution of patients with and without depression, as well as the above mentioned correlations, provide further evidence of the part played by organic factors in the cause of these syndromes.

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**Keywords:** neurocysticercosis; organic mental disorders; depression; psychosis

Neurocysticercosis is the most common parasitic infection of the human CNS<sup>1</sup> and is caused by the infection of nerve tissues by the larval form of the pork tapeworm *Taenia solium*. It occurs endemically in the rural areas of the

developing countries of Asia, Africa, Latin America, and central Europe, where prevalence rates vary from 0.1 to 4.0%.<sup>2-8</sup> It may also be found in urban areas of developed countries among ethnic subgroups.<sup>9-12</sup>

The two host life cycle of the cestode involves humans as definitive hosts and swine as intermediate hosts. The adult intestinal form of the parasite is acquired by eating undercooked pork contaminated with cysticerci,<sup>13,14</sup> whereas cysticercosis is usually acquired by a fecal-oral mechanism—that is, by the ingestion of *Taenia solium* eggs shed in the faeces of a human carrier. Contaminated water and food (especially raw vegetables) are the most common sources of infection.<sup>15,16</sup> The digested eggs release embryos that actively penetrate the mucosa of the upper digestive system and enter the blood stream. They lodge in muscle, fat, nerve, and eye tissues, and become encysted for several years.<sup>8</sup> The degeneration of the cysts, which may be spontaneous or induced by antiparasitic drugs, is accompanied by inflammation, fibrous encapsulation, and calcium deposition. Brain pathology is based on several different mechanisms, depending on the number, type, and location of the cysts, as well as the host's immune response.<sup>17-19</sup>

The clinical picture often includes seizures and hydrocephalus. Mental disturbances are typically present in the course of the disease and were extensively studied by psychiatrists at the beginning of the century. Mental syndromes that could mimic schizophrenia, major affective disorders, and dementia have been positively reported,<sup>20</sup> but few recent studies have tried to describe the psychopathology associated with neurocysticercosis with appropriate instruments for psychiatric assessment.

## Methods

In the present study, 38 non-selected consecutively admitted outpatients from the Section of Neuroinfectious Diseases of the Hospital das Clinicas—University of Sao Paulo (HCF-MUSP) were assessed between January 1993 and April 1994. The age range was restricted to between 18 and 60 years old. Patients with other neurological or medical conditions that could present psychiatric symptoms, as well as those on drug therapies that could affect the mental state (except the ones necessary for the treatment of epilepsy or intracranial hypertension) were excluded, as well as current alcohol and substance misusers.

Aetiological diagnosis was ascertained by

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positive immunological tests in CSF and tomographic findings suggestive of neurocysticercosis (small, multiple, and scattered calcifications or cystic, contrast enhanced or not, lesions within the brain parenchyma).<sup>15-17</sup> Brain MRI was performed to provide more sensitive imaging of patients with cystic lesions, both for diagnostic accuracy and detection of parenchyma oedema.<sup>21-23</sup>

Cases were classified according to the main site of lesion location in the CNS (parenchyma, ventricular, subarachnoid, and miscellaneous neurocysticercosis), and also according to disease activity.<sup>18</sup> Cases were considered inactive if neuroradiological images showed only calcifications or hydrocephalus without cysts, in the absence of signs of inflammation in the CSF analysis. Active disease included all cases in which cysts (with or without parenchyma inflammation) could be found in neuroimaging studies or cases with inflammatory CSF (increased CSF cells, pleocytosis, and increased protein concentrations).<sup>24</sup>

Current mental state was evaluated by the present state examination (PSE)<sup>25-26</sup> and the mini mental state examination (MMSE).<sup>27</sup> Previous psychiatric history was assessed with the schedule for affective disorders and schizophrenia—lifetime version (SADS-L).<sup>28-31</sup> A brief neuropsychological test was performed with Strub and Black's mental status examination (MSE),<sup>32</sup> which evaluates attention, memory, language (including reading and writing), visuospatial abilities, executive functions (including praxis and motor functions), and higher cognitive functions. Psychiatric diagnoses were based on the total PSE scores and allocation in the PSE syndromes and classes for each patient. Patients with suspected psychiatric disease were submitted to the DSM-III-R diagnostic criteria.<sup>33</sup> Due to the high prevalence of illiteracy among the users of the HCFMUSP facilities, different MMSE cut off points were used: 13 for the illiterate patients, 18 for those with four to eight years of schooling, and 26 for those with more than eight.<sup>34</sup>

## Results

All patients in the study were Brazilian (71% white, 7.9% black, and 21.1 half caste), mostly (60.5%) residents of urban areas (Greater Sao Paulo) and with low educational levels (66% had less than four years of instruction). Their ages ranged from 18 to 59 (mean 36.7), with no significant sex differences (47.4% men). There were four (10.5%) asymptomatic cases. Epilepsy was the most common presentation, found in 23 patients (60.5%). Six (15.8%) had hydrocephalus with intracranial hypertension, and five (13.2%) had focal symptoms without consistent evidence of intracranial hypertension. Although there were no patients with symptoms of meningitis, the CSF analysis of 17 patients (45.9%) disclosed signs of inflammation, 11 of whom (29.9%) also had positive antibody tests. No abnormalities were detected in the tests of the remaining 20 patients (54.1%) and one patient could not have his CSF analysed due to severe hydrocephalus.

Active neurocysticercosis was hence diagnosed for 29 patients (76.3%).

Radiographic data showed that 20 patients (52.6%) had parenchymal cysts or calcifications only. Ventricular and cysternal cysts occurred in five (13.2%), and the remainder had subarachnoid (5.3%) or miscellaneous lesions (28.9%). Parenchymal lesions were usually multiple and scattered, in different stages of evolution. Only five patients had a single cyst, 15 had two to five, and six had more than 20 brain lesions (one with more than 300). Both hemispheres were equally affected, including lesions in all cortical areas and subcortical structures (thalamus and basal ganglia).

Psychiatric diagnosis was based on previous (before this cross section) and current evidence of mental disease and also on signs of cognitive decline. Fifteen patients had no evidence of previous mental disease and 23 patients (60.5%) had a positive psychiatric history according to the SADS-L interview. Among these, 42 research diagnostic criteria (RDC) were met, which indicates that more than one diagnosis was possible for some patients in this lifetime assessment (table 1). Depressive disorders (including major, minor, and intermittent depression) were the most common of these findings (15 patients).

Thirteen patients (34.2%) were presumed mentally healthy by the PSE (index of definition < 5), whereas 25 (65.8%) had mild or moderate psychiatric manifestations compatible with at least one psychiatric diagnosis. The PSE subscores suggested that non-specific neurotic syndromes (NSNs) were possibly the main psychopathological tendency among the cases analysed, occurring in at least 75% of the test group, and achieving here the highest scores. The PSE subscores for specific neurotic syndromes (SNRs) and behaviour, speech, and others (BSOs) occurred in at least 25% of the observations, and delusions and hallucinations (DAH) in less than 25%. There were no patients with a typically schizophrenic presentation, although such psychotic symptoms were present in four cases (10.5%). Simple depression (SD) and loss of interest and concentration (IC) (23 patients, 60.5%), worry (WO) (22 patients, 57.9%), other depressive symptoms (OD) (19 patients, 50%), tension (TE) (18 patients, 47.4%), irritability (IT), and special depressive features (ED) (17 patients, 44.7%)

Table 1 Frequency of RDC/SADS-L diagnosis in 23 patients with neurocysticercosis

| RDC/SADS-L                      | n (%)     |
|---------------------------------|-----------|
| Major depression                | 12 (52.2) |
| Minor depression                | 1 (4.3)   |
| Intermittent depression         | 5 (21.7)  |
| Mania                           | 1 (4.3)   |
| Cyclothymia                     | 1 (4.3)   |
| Schizoaffective psychosis       | 3 (13.0)  |
| Panic disorder                  | 3 (13.0)  |
| Generalised anxiety disorder    | 2 (8.7)   |
| Simple phobia                   | 3 (13.0)  |
| Alcohol related problems        | 2 (8.7)   |
| Abnormal personality traits     | 2 (8.7)   |
| Unstable personality disorder   | 3 (13.0)  |
| Antisocial personality disorder | 1 (4.3)   |
| Attempted suicide               | 3 (13.0)  |

RDC/SADS-L = Research diagnostic criteria schedule for affective disorders and schizophrenia—lifetime version.

Table 2 Frequency of PSE classes ( $n = 38$ )

| PSE classes                           | $n$ (%)   |
|---------------------------------------|-----------|
| Retarded depression (R+)              | 10 (26.3) |
| Neurotic depression (N+/N?)           | 8 (21.2)  |
| Depressive psychosis (D+)             | 2 (5.3)   |
| Schizophrenic psychosis (S+/S?)       | 4 (10.5)  |
| Mania and mixed affective states (M+) | 1 (2.6)   |
| Non-specific symptoms (X)             | 6 (15.8)  |
| Normal examination (NO)               | 7 (18.4)  |

PSE = present state examination.

and loss of energy (LE) (15 patients, 39.5%) were the most common findings in the syndrome checklist.

Twenty patients (nine men and 11 women; 52.6%) had current signs of depression, if the three PSE classes retarded depression (R+), neurotic depression (N+, N?) and depressive psychosis (D+) were combined together (table 2). Eleven of those also had evidence of previous depression according to SADS-L and four patients had been depressed in the past but not at the time of the evaluation. Sixteen patients also met DSM-III-R diagnostic criteria for organic mood disorder with depressive features ( $k = 0.4$ ), providing further evidence of reliability for the PSE diagnosis of depression.

The distribution of MMSE scores ranged from 12 to 30 (mean 26.9; median 29). Only five patients (three of whom were illiterate) scored less than 20, and the maximum score of 30 points was achieved by 10 patients. When different cut off points were considered,<sup>34</sup> only two patients had MMSE performances worse than expected for their educational levels. However, the neuropsychological assessment of 32 patients suggested mild to moderate cognitive impairment in 23 (71.9%) and severe changes in five (15.6%). Six patients could not be evaluated because of illiteracy (three), visual deficits (two), and non-compliance (one). Attention deficits were detected in all the patients assessed by MSE (59.4% had mild to moderate and 40.6% severe attention disturbance). Memory, language, and higher cognitive functions were altered in 25, 25, and 28 patients respectively, and other deficits included praxis and motor functions (16 patients). Reading and writing skills were less often affected (nine and two patients respectively). However, there was no clear pattern of localisation for the neuropsychological dysfunctions in the patients of the test group.

Non-parametric statistical procedures were used to compare the PSE cases of depression (R+, N+, N?, D+) and psychosis (S+, S?, M+) with the non-depressed cases (X, NO). Pearson's  $\chi^2$  test was used for  $2 \times 2$  tables whenever possible; or alternatively Fisher's exact test was preferred when dealing with small numbers. Relative risk (RR) estimates (odds ratio (OR) with 95% confidence interval (95% CI)) were used to test the association between psychiatric variables (depression, psychosis, and cognitive state) and some possible risk factors for psychiatric morbidity. Patients in these groups did not differ significantly on most demographic characteristics, including age ( $F = 1.29$ , NS), sex ( $t = 1.59$ , NS), colour of skin ( $t = 0.91$ , NS), marital status ( $t =$

3.22, NS), educational level ( $t = 0.15$ , NS), and duration of neurological disease ( $t = 0.66$ , NS). No association was found between the use of steroids (11 patients) and current psychopathology, both for depression ( $P = 1.000$ ) and psychosis ( $P = 0.176$ ), nor between depression and severity of cognitive decline ( $P = 0.569$ ). The occurrence of depression correlated positively with disease activity as previously defined ( $\chi^2 = 4.062$ ,  $df = 1$ ,  $P = 0.044$ ;  $OR = 4.667$ , 95%  $CI_{OR} = 0.995-21.895$ ) and with the occurrence of intracranial hypertension ( $P = 0.118$ ;  $RR = 1.813$ , 95%  $CI_{RR} = 1.306-2.516$ ). Psychosis was also possibly associated with intracranial hypertension ( $P = 0.065$ ;  $RR = 5.333$ , 95%  $CI_{RR} = 1.923-14.790$ ) but not with disease activity ( $P = 0.500$ ). No association was found between the psychiatric manifestations and the occurrence of epilepsy ( $P = 0.629$ ). Ventricular and cysternal location of cysts also did not correlate with psychiatric variables ( $P = 0.621$ ) in the test group. Previous history of depressive disorders was strongly associated with current depression ( $\chi^2 = 7.620$ ,  $df = 1$ ,  $P = 0.006$ ;  $RR = 2.139$ , 95%  $CI_{RR} = 1.268-3.607$ ;  $OR = 14.667$ , 95%  $CI_{OR} = 1.590-135.322$ ) and psychosis ( $P = 0.044$ ;  $RR = 5.250$ , 95%  $CI_{RR} = 1.292-21.339$ ).

## Discussion

Very few publications have considered the psychiatric manifestations of neurocysticercosis, most of them consisting of anecdotal reports or brief descriptions of psychiatric cases in neurological studies.<sup>7 35-37</sup> Clear diagnostic criteria for the definition of psychiatric cases were not always used and less severe mental symptoms have probably been overlooked in such studies. Data from psychiatric research in neurocysticercosis are basically available from studies performed in mental institutions in the first half of the century, in which detailed clinical and pathological descriptions can be found.<sup>38-40</sup> Our study improves on these in some ways: (a) the choice of a sample of neurological outpatients made possible the investigation of psychiatric morbidity in patients with initial or mild forms of neurocysticercosis; (b) the use of semistructured interviews and diagnostic criteria provided a more reliable evaluation of current and previous mental status; (c) cognitive functioning was assessed by two instruments with different sensitivity levels; (d) clinical and radiological correlations were made, in the first attempt to identify possible risk factors of psychiatric illness associated with this organic disease.

The limitation of this study is that no control groups were used to decide if some of the psychopathological findings were greater than expected in other groups of non-neurological chronically ill patients or in those with a parasitic infection not involving the CNS. The first issue has been considered in other studies of neuropsychiatric conditions (such as stroke and multiple sclerosis), but no studies have attempted to describe the psychiatric complications of non-CNS cysticercosis. Such proce-

dures were beyond the initial scope of this cross sectional descriptive survey, but would definitely be a necessary methodological refinement for further studies. Also, the present sample was pathologically heterogeneous (lesions of different types were included) and patients were assessed only once, hence at different times in the outcome of a long term disease. Prospective follow up of selected patients with cystic lesions might detect further abnormalities at the time of the death of the parasite (treatment induced or not), which is a situation associated with greater CNS inflammation and consequently more clinical and possibly psychiatric implications.<sup>41</sup>

Our demographic data (available on request) are in agreement with the literature.<sup>36 42-47</sup> This study confirms that psychiatric manifestations are frequent in patients with neurocysticercosis. Prevalence rates vary greatly according to the origin of the patients and diagnostic accuracy.<sup>2 7 8 18 39 40 45 46 48-58</sup> The finding of 65.8% of mental abnormalities in our cross section is an estimate of the prevalence of psychiatric morbidity among neurological outpatients with neurocysticercosis. Samples of psychiatric inpatients might provide a different profile, with more severe or even specific forms of mental disease. Psychiatric surveys based on patients from mental institutions in the first half of the century reported up to 75% of severe mental disease in association with neurocysticercosis. Such a high rate might be explained by the duration of the untreated organic disease, as many of the patients had previous evidence of neurological syndromes before psychiatric admission.<sup>40</sup> Thus it is possible that mental disease represents one of the consequences of the deteriorating organic illness, in the absence of effective therapeutic strategies for neurocysticercosis at that time.<sup>8</sup> Moreover, mentally disabled patients may also be at an increased risk of developing neurocysticercosis, for they might become infected from the contact with faeces due to poor hygiene habits. Although it is a consensus that neurocysticercosis may be responsible for most of the major psychiatric syndromes (for example, schizophrenic and affective disorders) and dementia,<sup>7 20 38 39 43 49-51 59-66</sup> a particularly interesting finding of our study was the non-specific pattern of psychiatric morbidity, as shown by the PSE subscores. Very few studies have considered minor psychiatric manifestations or mild cognitive decline in patients with neurocysticercosis.<sup>35</sup> Possibly such syndromes were underestimated by most of the studies, which did not use instruments sensitive enough for an appropriate assessment, so that only the most dramatic cases of mental or behavioural changes were usually classified.

There was a high proportion of patients with depression (52.6%), which was the main psychopathological finding. Psychotic disorders were less frequent than previously reported, but this might again be explained by the use of a sample of neurological outpatients, who probably have less severe psychiatric disorders. History of mood disorder was strongly related to the occurrence of depression in the patients

from the test group and parallels several other studies on the aetiology of organic mood disorders. A family history of depression (which was positive in only three cases in the study) and a history of depression before the onset of the organic disease are regarded as risk factors for developing depression in cerebrovascular disease and multiple sclerosis, by means of a greater biological vulnerability.<sup>67 68</sup> The lack of significant sex differences among the PSE depressed patients is used by some authors as evidence of organic aetiology.<sup>68</sup> Further evidence could be the correlations between depression and disease activity and intracranial hypertension, provided we take into account that the test group was small in number. Other authors have already postulated from descriptive studies that intracranial hypertension was the syndrome most often related to psychiatric abnormalities in neurocysticercosis.<sup>2 53</sup> Disease activity (which is usually related to a diffuse or localised CNS inflammation) is possibly related to organic mood disorders, as shown in other medical and neurological conditions that affect the CNS, such as systemic lupus erythematosus<sup>69</sup> and multiple sclerosis,<sup>70</sup> but no attempts to correlate disease activity with depression have been made in patients with neurocysticercosis. Moreover, neurological symptoms in parenchymal neurocysticercosis seem to be positively related to the host's immune response,<sup>36</sup> and the onset of mental abnormalities has also been reported in the treatment of neurocysticercosis with antiparasitic drugs,<sup>71</sup> both situations associated with a greater CNS inflammation.

Finally, quite different outputs were obtained by MSE and MMSE (as expected), even after reallocation of patients according to education related MMSE cut off points, which could be explained by the greater sensitivity of the MSE. Both tests identified patients with severe cognitive decline, but only MSE was sensitive enough to detect minor neuropsychological abnormalities. Attention deficits were present in 100% of the MSE evaluations, probably being influenced by the effect of antiepileptic drugs (carbamazepine and barbiturates). Memory was also affected in a high proportion of patients, which is consistent with the findings of other authors<sup>39 50</sup> and reinforces the part played by neurocysticercosis in the cause of dementia.<sup>20 43</sup> Despite the lack of a proper controlled design for confounding variables (such as illiteracy, high prevalence of seizures, and use of anticonvulsant medication and steroids), this is to our knowledge the first attempt to describe the psychiatric manifestations in patients with neurocysticercosis by using standardised psychiatric instruments, as well as the first study to assess some possible risk factors for psychiatric morbidity associated with this cerebral disease. None the less, such findings clearly indicate the need for further exploration in this area.

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